REMARKS

Claims 5, 8, 25 and 26 are presently pending and all claims stand rejected. Applicants request the amendments of claims 25 and 26 as shown herein and addition of new claim 27. Claims 25 and 26 have been amended to recite antibodies or an assay utilizing said antibodies, wherein the antibodies specifically bind to fragments consisting of amino acids 6-30 of SEQ ID NO:2 or amino acids 7-30 of SEQ ID NO:2. Support for these amendments can be found, *inter alia*, at page 5, lines 1-26. The claims have been amended for the sake of clarity to recite any and all antibodies that "specifically" bind the disclosed fragments and to replace the claim language "all three of the glutamic acids at positions 17, 21 and 24" with "the glutamic acids at positions 17, 21 and 24." New claim 27 has been added. Support for this claim can be found, *inter alia*, at page 6, lines 1-5.

Interview of 10/14/03

The attorney for Applicants thanks the Examiner for the courtesy of conducting an interview in this matter, where the outstanding rejections were discussed. The claims have been amended in part based on the Examiner's acknowledgment that the written description guidelines and enablement requirements of 35 U.S.C. 112, first paragraph, do not require the deposit of an antibody species for adequate support of a generic claim to an antibody having a defined specificity.

Information Disclosure Statement

The Examiner has noted that a listing of the references in the specification is not a proper information disclosure statement. In response, the Examiner is referred to the Applicants' 1449 form submitted, with the cited references acknowledged by the Examiner and returned to Applicants' representative attached to Paper No.10. A copy of

the acknowledged references is attached.

Claim objections

The Examiner has objected to the ordered numbering of the claims and it is Attorney for Applicants understanding that further action on this objection will be delayed until allowable subject matter is established.

35 U.S.C. 112 second paragraph rejections

Claims 5, 8, 25 and 26 were rejected as indefinite because the Examiner is of the opinion that it is unclear what the claimed monoclonal antibody will bind and that this antibody will in fact bind to the full sequence of SEQ ID NO:2. The claims have been amended to recite antibodies or the use of said antibodies in immunoassays, wherein the antibodies specifically bind fragments consisting of amino acids 6-30 or amino acids 7-30 of SEQ ID NO:2.

Based on the amendments to the claims and the above comments, it is believed that all of the pending claims particularly point out and distinctly claim the elements of the invention and withdrawal of this grounds of rejection is requested.

35 U.S.C. 112 first paragraph rejections

Claims 5, 8, 25 and 26 were rejected for lack of an adequate written description. The Examiner is of the opinion that although the specifically disclosed antibodies are supported by adequate written description, the claims which recite antibodies that have the same binding activity of the disclosed antibodies but are not otherwise described lack adequate written description. It is Applicants understanding that this opinion was based in large part on the Examiner's belief that claims to a genus of antibodies having the same

binding characteristics require a deposit under the Budapest Treaty of one or more species of antibody from said genus. It is also Applicants understanding that this is not the case, and that the present claims to generic antibodies having a known structure and function, as exemplified by the disclosed species, are supported by adequate written description in the present specification. Such a conclusion is supported by the Synopsis of Application of Written Description Guidelines. These Guidelines note that a claim to "[a]n isolated antibody capable of binding to antigen X" is sufficient for § 112, paragraph one, compliance when antigen X is disclosed, considering "the well defined structural characteristics of the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature." The claims as amended recite antibodies which specifically bind the disclosed osteocalcin fragments. Furthermore, the specification discloses four antibodies of said genus, where none is required.

Based on the amendments to the claims and the above comments, it is believed that all of the pending claims are supported by adequate written description and withdrawal of this grounds of rejection is requested.

Claims 5, 8, 25 and 26 were also rejected for lack of enablement. The Examiner is of the opinion that "it is not clear that the properties of the...[specifically disclosed antibodies]...are known and publically available or can reproducibly be isolated from nature without undue experimentation..." The Examiner is further of the opinion that the "Applicant has not deposited the instantly claimed monoclonals." (Office Action of June 3, 2003, at page 11). In response, Applicants respectfully submit that the instant claims are directed to a generic antibody having the same binding activity as the disclosed monoclonals, *i.e.,* specificity for a fragment which consists of amino acids 6 to 30 or 7 to 30 of the amino acid sequence set forth in SEQ ID NO:2 in which the glutamic acids in

positions 17, 21 and 24 are gamma-carboxylated. The monoclonals representative of this genus are not, however, the instantly claimed monoclonals but instead represent examples of the claimed antibody that are not themselves claimed. Furthermore, since one of ordinary skill in the art could readily generate monoclonals as claimed without undue experimentation given the instant disclosure, a deposit is not required (MPEP 2402, 2404). In fact, the Examiner notes at page 11 of the outstanding Office Action that "the specification provides enough information for one of skill in the art to produce the same or similar properties" as the disclosed monoclonal antibodies.

Based on the amendments to the claims and the above comments, it is believed that all of the pending claims are enabled and withdrawal of this ground of rejection is requested.

Based on the above remarks and the amendments to the claims, it is believed that the claims satisfy the provisions of the patent statutes and that the present application is in condition for allowance. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,

Date: October 31, 2003

Michael J. Moran
Registration No. 42,013
Attorney for Applicants
Rothwell, Figg, Ernst & Manbeck, P.C.
1425 K Street, N.W., Suite 800
Washington, DC 20005
Telephone: (202) 783-6040
Fax: (202) 783-6031

Form 1449 — U.S. Department of Commerce, Patent and Trademark Office

ATTY. DOCKET NO.	SERIAL NO.
2328-115	09/462,931
APPLICANT: Jukka HELLMAN et al.	
FILING DATE: 07 January 2000	GROUP: 1641

LIST OF MATERIALS CITED BY APPLICANT
(Use several sheets if necessary)

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCL.	FILING DATE IF APPROPRIATE	
LVC	1	5 2 5 8 5 4 5	11-02-93	Kurihara et al.	560	162	5/22/92	
LVC	2	5 1 6 8 0 4 1	12-01-92	Bergmann	435	7.1	10/3/89	

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCL.	TRANSLATION	
							... YES	NO
LVC	3	8 3 4 7 4 0 A	04-08-98	EPO	G01N	33/53		
	4	5 5 7 6 6 3 A	09-01-93	EPO	G01N	33/68		
	5	5 0 4 4 2 3 A	09-23-92	EPO	G01N	33/53		
	6	4 1 8 6 1 7 A	03-27-91	EPO	CONSIDERED			
	7	9 7 3 8 3 0 9	10-16-97	PCT/Japan				x
① LVC	8	4 0 0 8 5 4 6	09-20-90	Germany		JUN 12 2000	x (abstract)	
① LVC	9	2 6 3 9 9 9	11-21-86	Japan		TECH CENTER 1600/2900	x (abstract)	
① LVC	10	2 0 9 5 9 6	08-31-88	Japan			x (abstract)	

NON-PATENT DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

LVC	11	Hellman, J. et al. (1996). "Epitope Mapping of Nine Monoclonal Antibodies Against Osteocalcin: Combinations into Two-Site Assays Affect Both Assay Specificity and Sample Stability," *J. Bone & Mineral Res.* **11**:1165-1175.
LVC	12	Nakao, M. et al. (1994). "Synthesis of Human Osteocalcins: γ-Carboxyglutamic Acid at Position 17 is Essential for a Calcium-Dependent Conformational Transition," *Peptide Res.* **7**:171-174.
LVC	13	Koyama, N. et al. (1991). "A one step sandwich enzyme immunoassay for γ-carboxylated osteocalcin using monoclonal antibodies," *J. Immunolog. Meths.* **139**:17-23.
LVC	14	Price, P. et al. (1987). "Molecular cloning of matrix Glas protein: Implications for substrate recognition by the vitamin K-dependent γ-carboxylase," *Proc. Nat. Acad. Sci. USA* **84**:8335-8339.

EXAMINER	DATE CONSIDERED
Lisa J. Cook	6/25/01

EXAMINER: Initial if reference considered, whether or not citation is in conformation with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

① English abstracts considered only LVC 6/25/01

Form 1449 U.S. Department of Commerce Patent and Trademark Office	ATTY. DOCKET NO. 2328-115	SERIAL NO. 09/462,931
LIST OF MATERIALS CITED BY APPLICANT (Use several sheets if necessary)	APPLICANT Jukka HELLMAN	
	FILING DATE 07 January 2000	GROUP 1641

Examiner Initial		NON-PATENT DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)
LVC	15	Celeste, A. et al. (1986). "Isolation of the human gene for bone gla protein utilizing mouse and rat cDNA clones," *EMBO J.* **5**:1885-1890.
LVC	16	Pan, L. et al. (1985). "The propeptide of rat bone γ-carboxyglutamic acid protein shares homology with other vitamin K-dependent protein precursors," *Proc. Nat. Acad. Sci. USA* **82**:6109-6113.

EXAMINER Lisa J Cook	DATE CONSIDERED 6/25/01

EXAMINER: Initial if reference considered, whether or not citation is in conformation with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.